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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,587	05/16/2001	Yoshiki Sasai	766.44	1416

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FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER

WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/855,587

Applicant(s)

SASAI ET AL.

Examiner

Joseph T. Voitach

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,12-15,18-24,26,27,56,57 and 72 is/are pending in the application.
- 4a) Of the above claim(s) 22,56 and 57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,12-15,18-21,23,24,26,27 and 72 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

This application claims benefit to provisional application 60/257,049, filed December 20, 2000, and to foreign applications: 1000-144059, filed May 16, 2000; and 2000-290819, filed September 25, 2000, both filed in Japan.

Applicants amendment filed March 11, 2004, has been received and entered. Claims 1, 22, 23, 56 and 57 have been amended. Claim 72 has been added. Claims 3-11, 16, 17, 25, 28-55 and 58-71 have been cancelled. Claims 1, 2, 12-15, 18-24, 26-27, 56, 57 and 72 are pending.

Election/Restrictions

Claims 1, 2, 12-15, 18-24, 26-27, 56, 57 and 72 are pending. Newly added claim 72 encompasses the use of specific cell lines in the elected invention, therefore will be examined with the elected invention. Claims 21, 56 and 57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13. See office action mailed January 16, 2003. It is noted that the election of species was required, in particular the species of (C) ectodermal cell (and generally with respect to the other species to cells of the nervous system) and the species of (Q) BMP4 was elected (see election page 2). Claims 1, 2, 12-15, 18-20, 22-24, 26-27 and 72 are currently under examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

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currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

"The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 12-15, 18-21, 23, 24, 26-27 previously rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn.

Claim 72 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention consists of use of specific cell lines (claim 72). It is noted that the claim indicates that the cells are a "stem cell", and to this end the specification and the art of record fails to provide a source or means to provide the specific stem cells claimed. More generally, since the cell lines are recited and thus required to be essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the cell lines are not so obtainable or available, the requirements of 35 U.S.C. 112, regarding "how to make", may be satisfied by a deposit of cell lines. Review of the specification by Examiner provides no indication as to public availability of the cell lines as stem

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cells or as stromal cells. Moreover, it is noted that names of the cells set forth in the claim can represent a variety of strains. For example cells termed NIH3T3 cells are well known in the art, however multiple strains each with varying characteristics have been described or are publicly available. In light of the intimate dependence of the claimed invention for the specific factor provided by the stromal cell. If deposits have been made and are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement.

It the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, Applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that

- (a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
 - (b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
 - (c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request for the effective life of the patent, whichever is longer; and,
 - (d) a test of viability of the biological material at the time of deposit (see 37 CFR 1.807);
- and,

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(e) the deposit will be replaced if it should ever become inviable.

Claims 1, 2, 12-15, 18-21, 23, 24, 26-27 and 72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

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As noted above, the election of species of differentiation into(C) ectodermal cells, in particular neural cells, and the use of the specific factor of (Q) BMP4 was elected. The basis of the rejection focuses on these two species and the evidence in the art that BMP4 acts as an antineuralizing morphogen. More specifically, At the time of filing Kawasaki *et al.* (Neuron 2000) teach that different stromal cells and cell lines can provide undefined factors termed SDIAs that allow for the differentiation of mouse ES cells (see summary in abstract). Review of the teaching of the instant disclosure provides similar guidance and examples as that provided by Kawasaki *et al.* Post filing art by Mizuseki *et al.* (PNAS, 2003) provide a similar teaching for the affect of BMP4 in the culture, however provides evidence that the affect of BMP4 is complex and dependent on the stromal cell used and the time that BMP4 is added to the co-culture. Both Kawasaki *et al.* and Mizuseki *et al.* teach that BMP4 when added to ES cells promotes epidermogenesis (Mizuseki *et al.*, page 5832, second column, Discussion section), not the formation of ectoderm cells or a more differentiated neural cell type. The post-filing evidence of Mizuseki *et al.* is noted, however there is nothing in the instant specification that would have led to the specific guidance or results presented by Mizuseki *et al.*

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 14, 18-21, 23, 24, 26, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (US patent 5,843,780).

Thomson teaches the isolation and maintenance of primate stem cells on stromal cells. More specifically, Thomson teaches the use of mouse STO cells as a feeder cells and does not teach to use RA in the culture media. Further, Thomson teaches that ES cells have the capacity to differentiate into any cell type and is evidenced by allowing the cells to form embryoid bodies or injecting the cells into a mouse to form a teratoma. It is noted that Thomson teaches that such conditions result in the maintenance of an undifferentiated ES cell, however the methods of Thomson anticipate the instant claims because there is not step in the pending claims to differentiate them from those set forth by Thomson. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or

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to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 1, 2, 14, 18-21, 23, 24, 26, 27 are rejected under 35 U.S.C. 102(a/e) as being anticipated by Samarut *et al.* (US patent 6,114,168).

Samarut *et al.* teaches the isolation and maintenance of primate stem cells on stromal cells. More specifically, Samarut *et al.* teaches the use of mouse STO cells as a feeder cells (column 3) and specifically teaches to exclude RA from the culture media (see summary in abstract). Further, Samarut *et al.* teaches that ES cells have the capacity to differentiate into any cell type and is evidenced by allowing the cells to form embryoid bodies or injecting the cells into a mouse to form a teratoma. As noted above for Thomson, Samarut *et al.* teaches that such conditions result in the maintenance of an undifferentiated ES cell, however the methods of Samarut *et al.* anticipate the instant claims because there is not step in the pending claims to differentiate them from those set forth by Samarut *et al.* Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "*prima facie* obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

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Claims 1, 2, 12-15, 18-24, 26-27, 56, 57 and 72 are rejected under 35 U.S.C. 102(a) as being anticipated by Kawasaki *et al.* (Neuron, 2000).

It is noted that the filing date is prior to the filing of the provisional application, and later than the foreign priority documents. However, a translation of the foreign priority documents has not been submitted and is not present in the file. In this case the priority date accorded the instant application is the filing date of the provisional application 60/257,049, filed December 20, 2000.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Yan *et al.* US 2002/0168763 A1, provides further evidence of culturing conditions for stem cells known in the art at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (571) 272-0734.

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Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

Joseph T. Voitach

Joe Voitach
AU1632